REMARKS

Claims 1-7 and 9-22 would remain pending following the entry of the above amendment. Claims 1 and 5 are the only independent claims. Previously pending claims 5-7 were deemed to be allowable in prior Office Actions.

The claims of the application have been amended to more particularly point out and distinctly claim the subject matter which Applicant regards as her invention.

Applicant appreciates the Examiner's time during the telephone interviews with the undersigned attorney during the evenings of October 20 and November 10, and on November 11 and 12, 1998, relating to prior drafts of informal proposed amendments of claim 1, as well as the submission on November 13 by FAX of the foregoing amendment to claims 1 and 5.

During the telephone interview of November 12, the Examiner indicated that an independent claim (amended claim 5 above) combining allowed claim 5 and the previously informally amended claim 1 would be allowable. During that same November 12 telephone interview, the Examiner indicated that another independent claim (amended claim 1 above) combining the previously informally amended claim 1 and dependent claim 8 would also be allowable if the claim recited that the absorbent did not remove the apolipoprotein from the delipidated fraction being returned to the subject. In a telephone message left by the Examiner on November 17, the Examiner stated that claims 1 and 5 as previously presented would be allowable and that the application would be in a condition for allowance if the application were otherwise cleaned up in accordance with the other amendments above, cancelling claim 8, which is now incorporated in claim 1, and changing the dependency of claims 9 and 11-13 which had depended from claim 8, to now depend from claim 1.

Initially, no new matter has been added to the application by the proposed amendments to independent claims 1 and 5. The retention of apolipoproteins in the treated blood fraction resulting from a cholesterol and other lipid apheresis process is a major distinguishing factor from a standard LDL apheresis technique, such as disclosed in U.S. patent 5,401,415 ("Rauch"), which specifically discloses removing such apolipoproteins (Rauh at column 4, lines 7-12 and 33-43, for example). The importance of retaining the apolipoproteins in the treated fraction returned to the subject in the present invention is disclosed at page 4, lines 10-18 of the

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application. By retaining such apolipoproteins, they are able to bind to, and in subsequent treatments remove, cholesterol and other lipids when the treated fraction is returned to the subject.

For establishing an antecedent basis for the later use of "blood cells", it is accurate to include the blood cells in the clause in line 4 of the amended claim 1 herein and in lines 4 and 5 of amended claim 5 herein reading "withdrawing blood containing blood cells from the subject". This renders the claim accurate, since the fraction is separated from the blood cells before the lipids are removed from the fraction.

Claims 1 and 5 also have been amended to indicate that the subject is connected to a device for withdrawing blood from a patient, and in a later clause, to make it clear that the solvent extraction step is carried out separately and remote from the subject while the subject is not still connected to the device for withdrawing blood from the subject. Clearly, the subject must be connected to some device of a type known in the art for withdrawing blood from the subject. See page 15, lines 2-6, of the application which indicates that patients have the plasmapheresis procedure undertaken using known transvenous techniques and plasmapheresis systems, such as by using vein-to-vein or arteriovenous fistula in the forearm of patients.

The performance of the solvent extraction separately and remote from the subject while the subject is not still connected to the device for withdrawing blood from the subject is clearly indicated at page 18, lines 24-25, specifically noting: "the patient whom no longer has to be hooked up to a delipidation apparatus for several continuous hours". See also page 15, lines 24-27, and page 18, lines 9-31 (and more specifically, lines 16-19), where reintroduction of the treated fraction into the patient is described as taking place after 12 hours following refridgeration of the fraction, and typically in accordance with the present invention, after one, two or several weeks. Unquestionably, one skilled in the art would know that a patient cannot be hooked up on line in a process like the process of the present invention for such a long time. That is what was meant by indicating that the invention "significantly reduces the contact time between the patient and the actual delipidation process" (page 7, lines 23-24), and by the use of the terms "discontinuous system" and "separately and remote" from the subject or patient or other similar terms, as used throughout the application, for example, at page 7, lines 11 and 30-

31; page 8, lines 7 and 13-15; page 16, lines 6-9 and 14-15; page 17, lines 19-23; page 18, lines 9-31; and in original claim 1 and in the Abstact of the Disclosure.

The last clause of amended claim 1 is also supported in the application. The importance of retaining the apolipoproteins in the treated fraction returned to the subject and its support is discussed above. If the absorbent were to remove the apolipoproteins from the treated fraction, the claimed method and the benefits of returning the apolipoproteins to the subject would not occur. See also the application at page 9, lines 3-7; page 9, line 13 - page 10, line 3; and the "Lipid Aphaeresis Procedure" at pages 12-13.

The telephone interviews with the Examiner of October 20 and November 10 and 11 were to discuss the language of amended claim 1 prior to combining it independently with claim 8 and with claim 5. Support for the amendments as discussed above was detailed, and the advantages of the present invention over the prior art were discussed

The advantages of the method of the present invention are that they overcome the disadvantages of the continuous lipid apheresis system of U.S. patent 4,895,558 ("Cham") set forth at pages 5-7 of the application, with the resulting corresponding advantages and other benefits set forth at page 17, line 19, through page 18, line 21. The advantages include separating the patient from the potentially explosive or otherwise dangerous solvents used in the solvent extraction step; being able to provide a reliable, multi-wash process for removing all of the solvent from the treated fraction before returning it to the patient, which cannot be done due to the restricted amount and flow of blood from a patient in the prior art continuous system of Cham; the ability to subject serum to delipidation and altered, improved rheology following delipidation treatment; and freeing the patient, equipment and medical staff for treating other patients or for dealing with other matters; among others.

During the telephone interviews of October 20 and November 10 and 11, the Examiner commented that he was aware of other extracorporeal blood treatment processes, where the blood is treated while the patient is not on line, such as those used to treat a patient's blood before it is returned to the patient a considerable time later, for example, following later-scheduled surgery. The undersigned attorney pointed out that such general extracorporeal processes usually simply add coagulants and are not involved with lipid apheresis, where the

apolipoproteins are retained in the blood fraction to be returned to the patient, while cholesterol and other such lipids are removed. The Examiner could not identify any particular process of the type he mentioned which involved the method claimed in the present application. The undersigned attorney further pointed out that if the discontinuous procedure of the present invention were so obvious, it would be used routinely, rather than subjecting patients receiving LDL apheresis or other such extracorporeal blood treatment procedures, even including Cham's procedure, to continuous procedures that require the patients to be continuously connected to the treating apparatus.

The Examiner also referred to Cham at column 2, lines 32-35, for Cham's disclosure of other prior art LDL apheresis techniques by the absorption of LDL onto heparin-agarose beads (affinity chromatography) or the use of immobilized LDL-antibodies. It was pointed out to the Examiner that these techniques would not adversely affect the patentability of the present application. Initially, that prior art disclosure in Cham refers to removing both the lipids including cholesterol, as well as the apolipoproteins, contrary to the method of the present invention. Further, heparin-agarose beads are unstable in organic solvents of the type used in the present invention and, if they were used in the method of claim 5, they would simply break up.

The blood fractions which are treated according to the present invention are unstable and accordingly, it is the practice in the art, including the Cham technique, to operate the treatment procedures on a continuous basis in which the blood is immediately returned to the patient while the patient remains connected to the treatment apparatus. The discontinuous procedure of the present invention allows a more rigorous treatment of blood than the continuous treatment procedure of Cham. Treating a blood fraction with an organic solvent without denaturing proteins, affecting pH, salt level and other critical blood parameters is a significant achievement. To be able to operate this system remotely from the patient, to treat the removed fraction not only once, but a number of times, if desired, and to store and otherwise treat the blood without adversely affecting the blood, are quite unexpected and go against the accepted procedures in the art. Any adversely affected blood cannot be tolerated, as this may be fatal to patients. The presently claimed invention is both novel and nonobvious compared to the prior art.

Since all claims are now believed to be in a condition for allowance, an early Notice of Allowance is respectfully requested. If the Examiner has any other questions or needs to discuss any other issues, the Examiner is respectfully requested to telephone the undersigned attorney.

Respectfully submitted,

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